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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,736	03/28/2000	Helge Bastian	C12Q1/68	5490
29425	7590	02/11/2004	EXAMINER	
LEON R. YANKWICH YANKWICH & ASSOCIATES 201 BROADWAY CAMBRIDGE, MA 02139			AKHAVAN, RAMIN	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/536,736

Applicant(s)

BASTIAN ET AL.

Examiner

Ramin (Ray) Akhavan

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22, 24-41, 44-51, 53-64 and 67-75 is/are pending in the application.
- 4a) Of the above claim(s) 6-8, 56 and 57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 9-22, 24-41, 44-51, 53-55, 58-64 and 67-75 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/2003 has been entered.

Concomitant to the request for continuing examination, applicant presents amendments to existing claims as well as new claims. Claims 1-22, 24-41, 44-64, 67-75 are pending with claim 6-8m 56-57 withdrawn from consideration as being directed to non-elected inventions. The claims under consideration are: claims 1-5, 9-22, 24-41, 44-51, 53-55, 58-64 and 67-75.

Response to Arguments

Applicant's arguments, see Remarks, filed 10/21/2003, with respect to Claim Rejections under § 112, ¶ 1 (incorporation of the term "non-siliceous" in the claims), have been fully considered and are persuasive. The *previous* rejection of claims 1-5, 9-22, 24-41, 44-50 and 59-64 under § 112, ¶ 1, has been withdrawn. All other objections and rejections not repeated herein are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-5, 9-22, 24-41, 44-51, 53-55, 58-64 and 67-75 are rejected under 35

U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Base claim 1 recites "immobilizing" where referring to nucleic acids and one side of the non-siliceous surface. It is unclear and indefinite what this means. For example the nucleic acids can be actually bound to the surface (e.g. membrane) or the nucleic acids can be entrapped or retained on the surface (e.g. through ultra-centrifugation). As written the claim is ambiguous thus making the metes and bounds of the invention indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-5, 9-14, 18-21, 24-26, 28-41, 44, 50 and 59-63 are rejected under 35

U.S.C. 102(b) as being anticipated by Mullis (US Patent 5,234,824).

Applicant argues in Remarks filed 10/21/2003, that this rejection is improper because Mullis does not teach a process wherein the nucleic acids do not penetrate to or make contact with the other opposing side of the non-siliceous surface.

Before discussing the argument, it would be helpful to summarize the subject matter to which the claims are drawn: a process for isolating nucleic acids comprising steps of charging the top side of a two sided non-siliceous surface, where nucleic acids are immobilized on one side and released from the same side and where nucleic acids do not penetrate through or make contact with the opposing side of the non-siliceous surface. The immobilization buffer can charge the membrane, contain alkaline, halogenides or sulfates or more specifically contain halogenides of sodium or potassium or magnesium sulfate. The nucleic acid may be washed in a buffer containing metal ion, chaotropic agent or alcohol. The releasing solution can be water, aqueous salt or buffer solution.

Mullis teaches a charging buffer that contains NaCl, Na₂HPO₄, KCl, SDS/PBS and MgCl₂, which is applied to a cellulose acetate membrane (non-siliceous), onto which nucleic acids are immobilized and subsequently washed with SDS/PBS and Tris chloride (50mM , pH 7.4). Nucleic acids are eluted by heating the filter immersed in water (col. 6, ll. 55-61), or Mullis teaches that a Tris chloride – MgCl₂ solution can be used (col. 8, ll. 1-8). As applicant points out the primary difference between Mullis and applicant's invention as amended is that the opposing surface of the membrane must not come into contact with nucleic acids released from the immobilized surface. (Remark, 10/21/2003, p. 19, l. 6; p. 20, middle ¶).

Applicant correctly points out that Mullis expressly teaches the membrane being physically immersed in elution buffer, thus applicant states, "It would be immediately evident to a person of ordinary skill in the art that immersing a filter containing DNA into an elution buffer...will result in both sides of the filter...contacting any DNA release from the filter." It is tacitly understood and clearly evident that the membrane in Mullis is not penetrated by nucleic

Art Unit: 1636

acids, so that the only real issue is whether there is contact between the opposing side and nucleic acids. However, with respect to eluted DNA “contacting” the opposing surface, one of ordinary skill in the art would expect that once the DNA is eluted, absent evidence to the contrary, it would not then reinitiate binding or make contact with the membrane, as the elution buffer would preclude such contact under the elution conditions.

Applicant’s also makes arguments with regard to differences between the instant claims and what is taught by Mullis. Specifically, applicant focuses on Mullis immersing the membrane and heating the membrane-containing eluant. Applicant is arguing limitations and embodiments that are simply not contained in the claims. Applicant is reminded that base claim 1 recites a process “comprising”, thus as long as the reference teaches what is claimed, irrespective of additional or different manipulations, then the claims are anticipated. In sum, applicant’s assertion is not deemed persuasive, as there is no *evidence* or convincing evidence that nucleic acids (as taught in Mullis), once released from the immobilized surface necessarily come into contact with the opposing surface of the non-siliceous membrane.

2. Claims 1-5, 9-14, 24-26, 28-30, 32, 39, 44, 50, 51, 58-60 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa et al. (EP 0431905 A1; hereinafter Ogawa).

Ogawa teaches a process for isolating DNA comprising applying a solution (triptone, NaCl and yeast extract) containing DNA and proteinase K to a membrane, which can be any commercially available membrane, for example polysulfone (non-siliceous). (e.g., col. 3, ll. 37-41). Ogawa teaches that washing with an appropriate buffer solution would increase yield, and

Art Unit: 1636

gives TE-buffer as an example. (e.g., col. 3, ll. 45-50). Ogawa also teaches that DNA is released from the membrane using shaking in a volume of TE buffer, where the eluate is recovered by pipette (without penetration through the membrane or contact with opposing surface). (e.g., col. 4, ll. 35-39). In sum Ogawa anticipates the rejected claims.

3. Claims 1-5, 9-14, 24-26, 28-30, 32, 39, 44, 50, 59-60 and 62 are rejected under 35 U.S.C. 102(b) as being Schneider (EP 0442026 A2).

Schneider teaches a process of isolating nucleic acids comprising charging a membrane with a cationic agent (Cetyl-trimethyl-ammonium bromide) where DNA is immobilized on a matrix (polypropylene or polyethylene), where the hydrophilic surface enables DNA to be recovered easily and speedily after washing operations, which include NaCl, ethanol and water. The DNA is eluted with aqueous solution or low ionic strength. (e.g. col. 2, ll. 30-55, bridging ¶¶ to col. 3). Therefore, Schneider anticipates the rejected claims.

4. Claims 1-3, 5, 24, 26, 28-29, 32, 39, 41, 50 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over rejected under 35 U.S.C. 102(a) as being anticipated by Millipore (Catalogue), 1995 (accessed on the web at URL: millipore.com/catalogue.nsf/docs/C7485) (last visited 02/07/04).

The claims are drawn to a process of isolating nucleic acids on one surface of a two-surfaced non-siliceous surface where the nucleic acids do not penetrate to or make contact with one side of the non-siliceous substrate. The average pore size for the surface is between 0.001 and 50 microns.

Only the top surface is contacted, where the nucleic acids are immobilized and release with intervening buffer washes if necessary. The immobilization buffer contains a chaotropic agent where the agent is between 0.01-10 molar aqueous solution, and a pH between 3 to 11. The releasing step is carried out using an aqueous salt or buffer solution. The immobilization buffer can contain salts of alkaline earth metals and metals with mineral acids, more spec

Millipore teaches isolating nucleic acids from the same surface where nucleic acids are immobilized through centrifugation onto a cellulose membrane (non-siliceous surface with average pore of 40 microns). (e.g., p. 2, under Protocol B). Nucleic acids are immobilized onto a cellulose (non-siliceous) membrane in an appropriate buffer (e.g. TE buffer; intrinsically between 0.1 and 1mM and pH of between 6-8). (Id.) Furthermore, Millipore teaches that the membrane can be washed before release of nucleic acids, where release is achieved by inverting the tube containing the sample and spinning to recover the isolated nucleic acid in the appropriate buffer (i.e. the nucleic acids never penetrate to or come into contact with the opposing surface of the non-siliceous membrane). Therefore the rejected claims are anticipated.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 1636

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

- 5. Claim 1-3, 5, 9-22, 24-32, 39, 41, 44-50 and 58-64 rejected under 35 U.S.C. 103(a) as being unpatentable over Millipore, 1995 (accessed on the web at URL: millipore.com/catalogue.nsf/docs/C7485) (last visited 02/07/04).**

In addition to the aforementioned subject matter, the claims are drawn to at least one chemical reaction carried out between release and removal of nucleic acids. Furthermore, the claims are drawn to the immobilization buffer or release buffer containing several different agents: salts of alkaline and alkaline earth metals with mineral acids, alkaline halogenides or sulfates, halogenides of sodium or potassium sulfate, organic acids, hydrocarbons, alkanols, phenols, water, acetates, cyanates, iodides, iodides and urea.

Millipore teaches using a cellulose membrane and discloses compatibility of the membrane with various chemical compounds, including acids/alkalis, organic solvents and other compounds. (e.g., Microcon Centrifugal Filter Device, pp. 8-9 ; available at URL : millipore.com/publications.nsf/docs/pf185). In addition Millipore teaches that DNA purification can be conducted using the disclosed membrane with appropriate buffers.

The ordinary skilled artisan seeking to isolate nucleic acids using the Millipore membrane would have been motivated to use commonly available and utilized chemical compounds in lysing and preparing cells containing desired nucleic acids, which could be isolated using the Millipore membrane. Furthermore, the nucleic acids immobilized on the membrane can undergo buffer exchange or washing before release from the membrane. In addition when releasing the nucleic acids a buffer containing various compatible chemical compounds could be used to retrieve the nucleic acids; e.g. acetic acid, sodium hydroxide, ammonium sulfate, chloroform, ethyl acetate, guanidine thiocyanate and urea (Microcon Centrifugal Device, at Table 4, p. 8). Given the teachings in Millipore and the level of skill of the ordinary skilled artisan at the time of applicant's invention, it must be considered that the artisan would have had a reasonable expectation of success in practicing the claimed invention (i.e. isolation of nucleic acids using the Millipore membrane with preparations containing various buffers) comprising different chemical compounds.

Conclusion


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can

Art Unit: 1636

be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


GERRY LEFFERS
PRIMARY EXAMINER